DEPARTMENT OF THE NAVY
BUREAU OF MEDICINE AND SURGERY
WASHINGTON, D C 20372-5120

IN REPLY REFER TO
BUMEDINST 3900.8
BUMED-02E
23 Jan 90

BUMED INSTRUCTION 3900.8

From: Chief, Bureau of Medicine and Surgery

Subj: WRITTEN ANIMAL USE PROPOSALS

Ref: (a) Public Law 99-198
(b) Animal Welfare Act (7 United States Code 2131 et seq)
(c) Title 9 Code of Federal Regulations 1, 2, and 3
(d) Federal Register, Part IV, Thursday, August 31, 1989, Department of Agriculture, Animal and Plant Health Inspection Service, Animal Welfare, Final Rules
(e) SECNAVINST 3900.38B

Encl: (1) General Instructions
(2) Study Protocol Format
(3) Training Protocol Format

1. Purpose. To establish procedures for developing and processing written proposals for the in-house use of animals in Navy Medical Department activities.

2. Background. Reference (a) recently amended reference (b) and became Federal law effective December 1986. This amendment instructed the U.S. Department of Agriculture (USDA) to rewrite and make specific changes to its animal welfare rules and standards (reference (c)). Proposed standards were published, and after a period allowed for public comment, modified rules (parts 1 and 2) were published as final in reference (d) with an effective date of October 30, 1989. This instruction implements the latest changes to the animal welfare rules that pertain to writing and reviewing protocols for animal use.

3. Applicability. This instruction applies to all procedures which use animals for:

a. Research, development, test, and evaluation (RDT&E).

b. Clinical investigation.

c. Diagnostic purposes.

d. Instructional programs or exhibitions.

4. Definitions

a. Protocol. A written plan which describes and justifies the use of animals. In this instruction, protocol refers to any of several different types of protocols which may be written (i.e., study protocol, training protocol, pilot protocol, standard operating procedures (SOPs), and addenda).

b. Study Protocol. A written proposal which identifies a specific research problem and describes, in detail, the experimental design proposed to provide answers to the problem. Several related experiments may be submitted together as a single study protocol; however, the scope of the proposal should be limited to work achievable within 1 or 2 years and adequate to provide data for publication as a scientific article.

c. Pilot Protocol. A written description of preliminary or exploratory research of very limited duration and scope. The pilot study may be used to evaluate the validity or feasibility of a new concept or procedure, to find the approximate dose response of a test compound, or to obtain information not otherwise available. Although data obtained from a pilot study may be helpful in creating a study protocol, this information would not likely be adequate for publication.

d. Training Protocol. A written justification and description for using animals to teach surgical or other medical procedures or principles. Every effort must be made to train as many students using the fewest number of animals possible.

e. Protocol Addendum. An addition or change to a protocol. An addendum will describe well-defined, substantive changes in the experimental design which will affect animal usage under an approved protocol.

f. Standard Operating Procedure (SOP). A description of a standardized method of accomplishing a task. SOPs may be written and approved for specific, often repeated techniques or procedures involving research animals (e.g., immunization routine, surgical catheter implantation), thus eliminating the need to readdress, in detail, animal use issues covered by the SOP when referenced in a study or pilot protocol.

g. Institutional Animal Care and Use Committee (IACUC). A committee established by written authority of the activity commanding officer to oversee all policies and procedures that relate to the humane use of animals for research, testing, or training. Membership and duties of the IACUC must conform to paragraph 2.31 of reference (d) and to reference (e).

5. Policy

a. The use of vertebrate animals for research, testing, or teaching will not begin until a written protocol has been reviewed and approved by the IACUC and the activity's commanding officer.

b. Objectives of a protocol should normally be obtainable within the anticipated tour of duty of the principal investigator.

(1) Active study protocols will be reviewed by the IACUC annually, or more often if desired by the IACUC.

(2) A training protocol may be approved for up to a 1-year period at a time, but must be limited to specific training objectives (e.g., four ATLS courses per year using six pigs to train 18 students during each course to perform six specified procedures: total 24 pigs authorized). If animal use procedures are basically unchanged, training protocols may be renewed for a second and third year by annually submitting an addendum for approval. After the third year, a new protocol must be prepared with updated information about the availability of alternative procedures and must be given critical review before being approved again.

c. Proposals involving the use of nonhuman primates will be staffed for review and approval per this instruction before being forwarded to the Bureau of Medicine and Surgery (MED-02E) for centralized review per reference (e). All other approved protocols will be sent to MED-02E for information and reference only.

d. The principal investigator must provide written assurance that animal use procedures do not unnecessarily duplicate previous experiments.

e. For any procedure likely to produce pain or distress to an animal, whether or not the discomfort is alleviated with anesthetics or analgesics, the principal investigator must document in the protocol that alternatives to those procedures were considered and found unsuitable. This narrative must identify the source of information, e.g., the Animal Welfare Information Center, used to determine that suitable alternatives were not available.

f. A veterinarian must be consulted during the planning of painful or stressful procedures to ensure that appropriate consideration is given to the use of tranquilizers, analgesics, anesthetics, or euthanasia to minimize animal discomfort. If

these agents must be withheld because of scientific necessity, the principal investigator must provide a satisfactory justification and must withhold them for only as long as is absolutely necessary.

g. Paralytic agents will not be used without adequate anesthesia.

h. No animal will be used in more than one major operative procedure from which it is allowed to recover unless the justification written in the protocol complies with one of the exceptions listed in paragraph 2.31(d)(x) of reference (d) and is approved by the IACUC.

i. Any and all exceptions to USDA standards for the humane handling, care and treatment, and transportation of animals must be documented in detail in the protocol and scientifically justified to the satisfaction of the IACUC.

j. A protocol addendum will be used to request any additional expenditure of resources (e.g., number of animals) or any change in animal use procedures necessary to complete or continue an approved animal use protocol. Addenda must also be reviewed and approved by the IACUC and the activity's commanding officer before it is implemented.

6. Responsibility

a. The commanding officer will:

(1) Appoint appropriate members to the IACUC in writing.

(2) Approve or disapprove appropriately staffed, reviewed, and approved research protocols and authorize the use of activity resources to accomplish approved research. The commanding officer may not overrule an IACUC disapproval.

(3) Ensure that all activity animal use complies with approved protocols.

b. Department heads will establish a mechanism for critical review of protocols generated from within their respective departments prior to submission to the IACUC. Departmental review will ensure that protocols are in the proper format, are of the highest technical and scientific quality, and comply with appropriate regulations or instructions. Critical review of a proposal will enhance its quality and speed its approval.

c. IACUC chairman (or other person designated by the commanding officer) will:

(1) Schedule the activities of the committee to include protocol review and semiannual inspections as detailed in references (d) and (e).

(2) Notify in writing the principal investigator and the commanding officer of the committee's decision to approve or disapprove each protocol. A disapproval will be justified, and the principal investigator will be permitted to present new or more convincing information to the committee for reconsideration.

(3) Assign sequential accession numbers to approved protocols. This number will be used to monitor progress and animal usage.

(4) Maintain the official file of approved protocols, the minutes of pertinent committee meetings, and other documents or materials that relate directly to approved protocols.

7. Procedure

a. Investigators will write their protocols using language which is easily understood by scientists of other disciplines or by reasonably well-educated laymen.

(1) Investigators are encouraged to consult other scientists when creating their protocols. A veterinarian must be consulted if proposed procedures are likely to cause pain or distress to animals (paragraph 5f). Other activities which will be expected to supply support or services (e.g., animal resources, pathology, statistics) will also be consulted. Coordination will be documented on the signature page of the protocol.

(2) Protocols should follow a standardized format similar to that contained in enclosures (1) through (3). Exceptions to the format are permitted to meet regulatory requirements (e.g., good laboratory practice (GLP) compliant studies).

(3) Addenda and pilot studies may use a simplified format (memorandum) which describes and justifies the proposed changes or procedures.

(4) SOPs are internal documents; therefore, the format of SOPs will be dictated by the appropriate department head.

b. The department head will initiate the departmental process (paragraph 6b) to critically review the protocol for scientific merit and design, military relevance, compliance with regulations and standards, adequate coordination, and adequate animal use documentation. The department head is encouraged to invite unbiased individuals from outside the department to participate in the review.

(1) The author will rewrite the protocol to address appropriate criticisms to the satisfaction of the department head.

(2) The department head will forward the revised study protocol to the IACUC chairman for consideration at the next scheduled IACUC meeting.

c. The IACUC will meet regularly, as necessary, to consider submitted protocols.

(1) A quorum (majority of members) must be present. The IACUC chairman will prepare minutes of all meetings and have them approved by the commanding officer. Principal investigators who have had protocols considered must be expeditiously notified of the committee's recommendations. However, it should be clearly noted that approval by the committee does not constitute final approval (see paragraph 7e.)

(2) Under rare and exceptional circumstances it may be necessary to gain the opinion of the committee without convening a formal meeting (e.g., for expedited review). In such a case, the protocol will be forwarded by the IACUC chairman to committee members for their recommendations. Comments and recommendations will be returned to the chairman per the chairman's instructions (e.g., in writing or by phone). Minutes will reflect the method of committee deliberations and the committee's recommendations. If any committee member requests a formal review, a quorum of the IACUC must meet to discuss the protocol.

d. If the committee does not recommend immediate approval, the author will revise the protocol as necessary to comply with the committee's recommendations. Optionally, if the author does not concur with the committee's recommendations, the author may resubmit the protocol, presenting new information which may sway the opinion of the committee.

e. The author will submit four copies of the final amended draft protocol to the IACUC chairman. One copy will be clearly marked to highlight those changes required by the IACUC. If the chairman feels that issues were adequately addressed, the protocol will be forwarded to the commanding officer, recommending final approval. If the chairman is concerned that the changes do not adequately address the committee's criticisms, the protocol will be resubmitted for full committee review.

f. If a protocol involves the use of nonhuman primates, the commanding officer must forward it to MED-02E for centralized review (reference (e)) prior to granting final approval.

g. Once final approval is granted by the commanding officer, the IACUC chairman will assign an accession number to the protocol. This number will be the primary means of identifying the protocol when ordering animals. One copy of the signed, approved protocol will be provided to the necessary offices controlling the procurement and care of animals.

h. Only animals authorized by the commanding officer will be purchased, obtained, or used. One copy of the signed, approved protocol will be forwarded to MED-02E for information and reference.

8. Form. DD 1498 (3-83), Research and Technology Work Unit Summary, S/N 0102-LF-014-9301, is available from the COG 1I stock points of the Navy Supply System, and can be ordered per NAVSUP P-2002.

Robert W. Higgins

ROBERT W. HIGGINS
Acting

Distribution:
SNDL, 21A (CINCS)
23A2 (COMNAVFORJAPAN, COMNAVMARIANAS only)
28CS (COMNAVSURFGRU LONG BEACH only)
28K1 (COMSUBGRU TWO only)
42A1 (COMFAIRCARIB, COMFAIRKEFLAVIK)
42A2 (COMFAIRMED)
42B1 (COMHELWINGSLANT only)
42B2 (COMMATVAQWINGPAC, COMPATWINGSPAC only)
C28H (BRMEDCLINIC)
C28G (BRDENCLINIC)
C31J (BRMEDCLINIC)
C31K (MEDADMINU)
C34F (BRMEDCLINIC & MEDCLINIC, LONDON DET)
C34G (BRDENCLINIC)
C52 (BUMED SHORE BASED DETACHMENTS)
C58Q (BRDENCLINIC)
C58R (BRMEDCLINIC
C85A (BRMEDCLINIC)
FA6 (NAS KEY WEST only)
FA24 (COMNAVBASE CHARLESTON, GUANTANAMO BAY, NORFOLK, and PHILADELPHIA only)
FA47 (NAVHOSP)
FA48 (DENCLINIC)
FA49 (MEDCLINIC)
FB28 (COMNAVBASE PEARL HARBOR, SAN DIEGO, SAN FRANCISCO, and SEATTLE only)
FB50 (COMUSFAC)

FB58 (NAVHOSP)
FB59 (DENCLINIC)
FB60 (MEDCLINIC)
FC3 (COMNAVACT UK only)
FC16 (MEDCLINIC)
FC17 (NAVHOSP)
FC18 (DENCLINIC)
FF1 (COMNAVDIST)
FH (BUMED COMMAND ACTIVITIES)
FT1 (CNET)
FT2 (CNATRA)
FT5 (CNTECHTRA)
FT28 (NETC)
FT31 (NTC GREAT LAKES, ORLANDO only)
FT108 (NAVHOSP)
FT109 (DENCLINIC)
FT110 (MEDCLINIC)
FW1 (NATNAVMEDCEN)
FW2 (NATNAVDENCEN)
FW3 (NAVHOSP)
FW4 (MEDCLINIC)
V3 (COMCABEAST only)
V8 (CG MCRD PARRIS ISLAND only)
V16 (CG MCB CAMP BUTLER, CAMP LEJEUNE, and CAMP PENDLETON only
V25 (CG MCAGCC)

Stocked:
CO, NAVPUBFORMCEN
5801 Tabor Ave.
Phila., PA 19120-5099

GENERAL INSTRUCTIONS

1. Written animal use protocols are required by references (d) and (e). Research using animals will not commence until a protocol has been approved by an IACUC and the performing activity's commanding officer.

2. The protocol will be written in clear, concise language, easily understood by a college graduate without specialty training. Common medical terminology is acceptable.

3. Normally, a well-written protocol will address all required topics adequately without exceeding 10 pages.

4. Approved protocols are releasable under the Freedom of Information Act. Since statements or phrases from released documents are sometimes used out of context by special interest groups, protocols should be carefully prepared.

5. Pages will be numbered consecutively with arabic numerals at the bottom center of the page, beginning on page 2.

6. A recognized style for using scientific or other abbreviations and for citing references should be used. If a study is to be published, the author should use the style recommended by the publisher.

b. Other information to be included in the Materials and Methods section:

(1) Identify the animal models (species, breed, strain, sex, age or weight, and other pertinent information) to be used and justify their appropriateness.

(2) Justify the number of animals of each species to be used. This is best accomplished by explaining the protocol design, describing the various study groups, and explaining the statistical plan for analysis of data. Since the IACUC can authorize only the number of animals properly justified, explain why additional animals might be needed for pilot studies or likely complications (e.g., poor recovery rates from complicated surgery, predicted catheter failures, etc.).

(3) Describe the procedures or treatment to which animals will be subjected. If surgical procedures are to be employed from which animals are expected to recover, indicate that aseptic techniques will be used and address pre- and post-surgical care. Describe when and how euthanasia will be performed.

(4) Exceptions to compliance with chapter 1, subchapter A of reference (c) may be made only when necessary to accomplish the research design and when specified in the protocol and justified to the satisfaction of the IACUC. These exceptions must be explained as part of the annual report to USDA.

(5) If hazardous agents (radioisotopes, infectious agents, or hazardous chemicals) are to be used, describe precautions to be observed to protect individuals or other animals.

5. References. List in order cited. References must reflect a thorough knowledge of current literature on the subject.

6. Signature Page

a. Provide the following declaration:

"I agree that research animals assigned to this protocol will be used only as described. I recognize my responsibility to consider alternatives to procedures which cause pain or discomfort to animals. I also understand that pain or discomfort must be minimized, to include the use of tranquilizers, analgesics, and anesthetics, as appropriate. Exceptions to these and other USDA standards are described and justified in full."

b. Signatures below imply concurrence:

(1) Signature of principal investigator.

STUDY PROTOCOL FORMAT

1. Administrative Section. Information which specifically identifies the protocol:

a. A concise but informative title typed in capital letters.

b. Name of the principal investigator followed by a list of other major contributors.

c. Name of the branch, division, or department from which the research is originating.

d. Other information which may help to identify or process the protocol (e.g., DD 1498, Work Unit Number, accounting classification codes, and other information specified by the commanding officer).

2. Background or Introduction. Clearly justify the rationale for the research and concisely discuss relevant facts and suppositions bearing on the problem. Demonstrate with references a thorough familiarity with current, pertinent literature on the subject. This description must be convincing that the information being sought is relevant and important, and that the research does not unnecessarily duplicate other work.

3. Hypothesis. Clearly state the hypothesis or null-hypothesis. Results of data analysis must either support or reject the hypothesis. Occasionally, research does not lend itself to testing a specific hypothesis (e.g., range finding pilot protocol), in which case specific research objectives will be stated.

4. Materials and Methods

a. Describe the experimental design in sufficient detail that reviewers can thoroughly evaluate the scientific merit of the approach. Procedures which are likely to cause pain or discomfort to animals, whether or not drugs are used to alleviate the discomfort, must be thoroughly described and the following points addressed:

(1) Explain the rationale for using animals vice nonanimal alternatives.

(2) Describe the techniques to be used to minimize pain or discomfort. Be specific: name drugs, dosages, routes of administration, and frequency of administration. Withholding pain relief is permitted only if scientifically necessary; omission must be convincingly justified.

objectives and when specified and adequately justified in the protocol. These exceptions must be explained as part of the annual report to USDA.

4. References. List any references which strengthen the justification for the training or the procedures used.

5. Signature Page

a. Provide the following declaration:

"I agree that research animals assigned to this protocol will be used only as described. I recognize my responsibility to consider alternatives to procedures which cause pain or discomfort to animals. I also understand that pain or discomfort must be minimized, to include the use of tranquilizers, analgesics, and anesthetics, as appropriate. Exceptions to these and other USDA standards are described and justified in full."

b. Signatures below imply concurrence:

(1) Signature of course director.

(2) Signature of other course contributors.

(3) Signatures of providers of in-house support.

(4) Signature of consulting veterinarian.

(2) Signatures of coinvestigators.

(3) Signatures of providers of in-house support.

(4) Signature of consulting veterinarian.

TRAINING PROTOCOL FORMAT

1. Administrative Section. Information which specifically identifies the protocol:

a. A concise, but informative title typed in capital letters.

b. Name of course director and other major contributors.

c. Name of branch, division, or department sponsoring the course.

d. Other information which may help identify the course and is required by the commanding officer.

2. Introduction. Provide an overview of the proposed training. Describe the training objectives and indicate their medical application. Include the number and type of students expected to be trained and list the procedures to be covered. Justify why animal use is essential and explain what non-animal alternatives were considered and why they are not suitable replacements.

3. Plan. Describe the teaching strategy in sufficient detail that reviewers can evaluate the merit of the approach. If multiple procedures are to be taught or demonstrated, give a step-by-step sequence of events (a flow chart may be helpful). The following animal use issues must be addressed:

a. Identify the animal models to be used (species, breed, strain, sex, age or weight, and other pertinent information). Justify the appropriateness of the model.

b. Indicate and justify the number of animals of each species to be used. Use the fewest number of animals that will accomplish the training objective.

c. Describe the procedures or treatment to which animals will be subjected. If surgical procedures are to be used from which animals will be expected to recover, aseptic techniques must be used. Address this and the provisions for pre- and post-surgical care. Describe when and how euthanasia will be performed.

d. Describe the techniques proposed to minimize animal pain or discomfort. Name drugs, dosages, routes of administration, and frequency of administration. Withholding pain relieving drugs is permitted only if scientifically necessary and justified to the satisfaction of the IACUC.

e. Any exceptions to compliance with reference (c) may be made only when scientifically necessary to accomplish the training